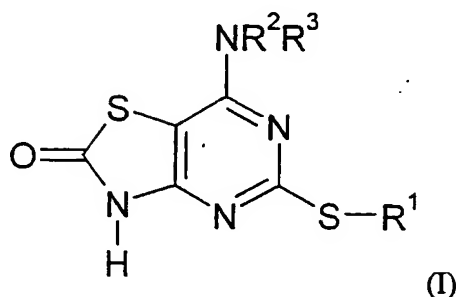


## CLAIMS

1. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof:



in which

- $R^1$  represents a  $C_3$ - $C_7$  carbocyclic,  $C_1$ - $C_8$  alkyl,  $C_2$ - $C_6$  alkenyl or  $C_2$ - $C_6$  alkynyl group, each of the groups being optionally substituted by one or more substituent groups independently selected from halogen atoms,  $-OR^4$ ,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$  or an aryl or heteroaryl group, both of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro,  $-OR^4$ ,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ ,  $C_1$ - $C_6$  alkyl or trifluoromethyl groups;

$R^2$  and  $R^3$  each independently represent a hydrogen atom, or a  $C_3$ - $C_7$  carbocyclic,  $C_1$ - $C_8$  alkyl,  $C_2$ - $C_6$  alkenyl or  $C_2$ - $C_6$  alkynyl group, the latter four groups may be optionally substituted by one or more substituent groups independently selected from:

- (a) halogen atoms,  $-OR^4$ ,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$
- (b) a 3-8 membered ring optionally containing one or more atoms selected from O, S,  $NR^8$  and itself optionally substituted by  $C_1$ - $C_3$ -alkyl or halogen,
- (c) an aryl group or heteroaryl group each of which may be optionally substituted by one or more substituents independently selected from halogen atoms, cyano, nitro,  $-OR^4$ ,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-NR^8COR^9$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ ,  $C_1$ - $C_6$  alkyl and trifluoromethyl groups;

R<sup>4</sup> represents hydrogen, C<sub>1</sub>-C<sub>6</sub> alkyl or a phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR<sup>11</sup> and -NR<sup>12</sup>R<sup>13</sup>

- 5 R<sup>5</sup> and R<sup>6</sup> independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub> alkyl or phenyl group the latter two of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl, -OR<sup>14</sup> and -NR<sup>15</sup>R<sup>16</sup>, -CONR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>COR<sup>16</sup>, -SONR<sup>15</sup>R<sup>16</sup>, NR<sup>15</sup>SO<sub>2</sub>R<sup>16</sup>

or

- 10 R<sup>5</sup> and R<sup>6</sup> together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system optionally containing a further heteroatom selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl, -OR<sup>14</sup>, -COOR<sup>14</sup>, -NR<sup>15</sup>R<sup>16</sup>, -CONR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>COR<sup>16</sup>, -SONR<sup>15</sup>R<sup>16</sup>, NR<sup>15</sup>SO<sub>2</sub>R<sup>16</sup> or C<sub>1</sub>-C<sub>6</sub> alkyl, itself  
15 optionally substituted by one or more substituents independently selected from halogen atoms and -NR<sup>15</sup>R<sup>16</sup> and -OR<sup>17</sup> groups;

- R<sup>10</sup> represents a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub>-alkyl or a phenyl group, the latter two of which may be optionally substituted by one or more substituent groups independently selected  
20 from halogen atoms, phenyl, -OR<sup>17</sup> and -NR<sup>15</sup>R<sup>16</sup>; and

each of R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>11</sup>, R<sup>12</sup>, R<sup>13</sup>, R<sup>14</sup>, R<sup>15</sup>, R<sup>16</sup>, R<sup>17</sup> independently represents a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub>, alkyl, or a phenyl group.

- 25 2. A compound according to claim 1, wherein R<sup>1</sup> represents an optionally substituted benzyl group.

- fresh*  
*A1*  
30 3. A compound according to claim 1 or claim 2, wherein one of R<sup>2</sup> and R<sup>3</sup> is hydrogen and the other is C<sub>1</sub>-C<sub>8</sub> alkyl substituted by hydroxy and one or more methyl or ethyl groups.

4. A compound according to claim 1 selected from:

7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-2(3H)-one,

(*R*)-7-[[1-(Hydroxymethyl)propyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

(*R*)-7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

5 5-[[2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

5-[[2,3-Difluorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

10 5-[[2,3-difluorophenyl)methyl]thio]-7-[[2-(hydroxyethoxy)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

5-[[2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

7-[(2-aminoethyl)amino]-5-[[2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

15 5-[[2,3-difluorophenyl)methyl]thio]-7-[(2-hydroxyethyl)amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

*N*-[2-[[5-[[2,3-difluorophenyl)methyl]thio]-2,3-dihydro-2-oxothiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethyl]methanesulfonamide,

20 (+/-)-5-[[2,3-difluorophenyl)methyl]thio]-7-[[2-(2-hydroxyethoxy)-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

7-[[2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

5-[[2,3-difluorophenyl)methyl]thio]-7-[(1*R*)-2-[(2-hydroxyethyl)amino]-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

25 5-[[2,3-difluorophenyl)methyl]thio]-7-[(1*R*)-2-(dimethylamino)-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

5-[[4-(2-aminoethoxy)-3-chlorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

30 5-[[3-Chloro-4-methoxyphenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

- 5-[[3-Chloro-2-fluorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[[2,3-Difluorophenyl)methyl]thio]-7-[[3*R*,4*R*)-4-hydroxypyrrolidin-3-yl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[[2,3-Difluorophenyl)methyl]thio]-7-[(3*R*)-pyrrolidin-3-ylamino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[(1*R*)-2-Hydroxy-1-methylethyl]amino]-5-[[2-methyl-4-thiazolyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[[2-Hydroxy-1-(hydroxymethyl)ethyl]amino]-5-[[2-methyl-4-thiazolyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[[2-methyl-4-thiazolyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[[2-methylphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[(2-Furanylmethyl)thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[(1*R*)-2-Amino-1-methylethyl]amino]-5-[[3-chloro-2-fluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one
- (2*S*)-2-[[5-[[2,3-Difluorophenyl)methyl]thio]-2,3-dihydro-2-oxothiazolo[4,5-*d*]pyrimidin-7-yl]amino]-3-hydroxy-propanamide,
- 7-[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(2-thienylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 7-[(1*R*)-2-hydroxy-1-methylethyl]amino]-5-[[3-methyl-4-(methylsulfonyl)phenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[[[3-chloro-4-(trifluoromethoxy)phenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[[[2-fluoro-3-(trifluoromethyl)phenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,
- 5-[[2,3-difluorophenyl)methyl]thio]-7-[2-[(dimethylamino)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,

- 5-[[ (2-fluorophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino]-5-[[ (2-methoxyphenyl)methyl]thio] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5 7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino]-5-[(2-phenoxyethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino]-5-[[ (3-methylphenyl)methyl]thio] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5-[[ (2-fluoro-3-methylphenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
10 5-[[ (3-chlorophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5-[[ (3-bromophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
15 5-[[ [4-(difluoromethoxy)phenyl]methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
(+/-)-5-[[ (2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(methoxymethyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
20 5-[[ (2-bromophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5-[[ (2,3-Difluorophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
25 5-[[ [3-Chloro-2-fluorophenyl)methyl]thio]-7-[[ (1*R*)-2-hydroxy-1-methylethyl]amino] thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
(+/-)-5-[[ (2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(methoxymethyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
30

- 7-[(1*R*)-2-Hydroxy-1-methylethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5-[(5-chloro-1,2,3-thiadiazol-4-yl)thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]-thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
5 and their pharmaceutically acceptable salts and solvates.

5. A compound according to claim 1 selected from:

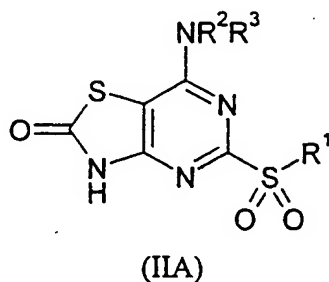
- 5-[(2,3-Difluorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one sodium salt,  
10 5-[[3-Chloro-2-fluorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one sodium salt,  
(+/-)-5-[(2,3-difluorophenyl)methyl]thio]-7-[[2-hydroxy-1-(methoxymethyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one sodium salt,  
7-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one sodium salt, or  
15 7-[(1*R*)-2-Hydroxy-1-methylethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one sodium salt.

6. A compound according to claim 1 selected from:

- 20 7-[(1*R*)-2-amino-1-methylethyl]amino]-5-[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one trifluoroacetate,  
5-[(2,3-difluorophenyl)methyl]thio]-7-[(1*R*)-2-[(2-hydroxyethyl)amino]-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one trifluoroacetate,  
5-[(2,3-difluorophenyl)methyl]thio]-7-[(1*R*)-2-(dimethylamino)-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one,  
25 5-[[[4-(2-aminoethoxy)-3-chlorophenyl)methyl]thio]-7-[(1*R*)-2-hydroxy-1-methylethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one trifluoroacetate,  
5-[(2,3-difluorophenyl)methyl]thio]-7-[2-[(dimethylamino)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one monohydrochloride, or  
30 5-[(2,3-Difluorophenyl)methyl]thio]-7-[(3*R*)-pyrrolidin-3-ylamino]thiazolo[4,5-*d*]pyrimidin-2(3*H*)-one dihydrochloride.

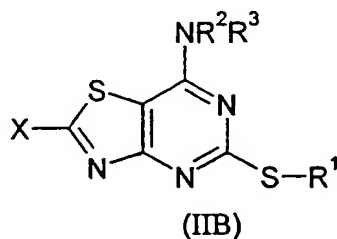
7. A process for the preparation of a compound of formula (I) as defined in claim 1 which comprises:

(a) treating a compound of formula (IIA):



where  $R^1$ ,  $R^2$  and  $R^3$  are as defined in formula (I) with a thiol  $R^1SH$  in the presence of a suitable base, or

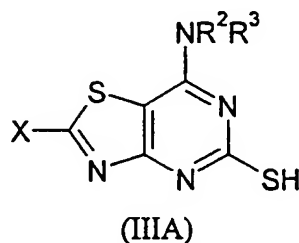
(b) treatment of a compound of formula (IIB):



where  $R^1$ ,  $R^2$  and  $R^3$  are as defined in formula (I) and X is a leaving group with a metal alkoxide, followed by treatment with an acid or base, and optionally after (a) or (b) forming a pharmaceutically acceptable salt.

8. A compound of formula (IIA) or (IIB) as defined in claim 7.

9. A compound of formula (IIIA):



where  $R^2$  and  $R^3$  are as defined in formula (I) and X is  $NH_2$

10. A pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1 to 6  
5 in association with a pharmaceutically acceptable adjuvant, diluent or carrier.
11. A process for the preparation of a pharmaceutical composition as claimed in claim 10  
10 which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1 to 6 with a pharmaceutically acceptable adjuvant, diluent or carrier.
12. A compound of formula (I), or a pharmaceutically-acceptable salt or solvate thereof, as  
claimed in any one of claims 1 to 6 for use in therapy.
13. Use of a compound of formula (I), or a pharmaceutically acceptable salt or solvate  
15 thereof, as claimed in any one of claims 1 to 6 in the manufacture of a medicament for use in therapy.
14. A method of treating a chemokine mediated disease wherein the chemokine binds to  
20 one or more chemokine receptors, which comprises administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1 to 6.
15. A method according to claim 14 in which the chemokine receptor belongs to the CXC  
25 chemokine receptor subfamily.
16. A method according to claim 14 or 15 in which the chemokine receptor is the CXCR2  
receptor.
17. A method of treating an inflammatory disease in a patient suffering from, or at risk of,  
30 said disease, which comprises administering to the patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as claimed in any one of claims 1 to 6.
18. A method according to claim 17, wherein the disease is psoriasis, a disease in which  
35 angiogenesis is associated with raised CXCR2 chemokine levels, or COPD.



**Figure 6.** The effect of the initial concentration of the monomer ( $C_0$ ) on the polymerization rate at different temperatures. The reaction conditions were as follows:  $[AIBN] = 0.008 \text{ mol/L}$ ,  $[M] = 0.001 \text{ mol/L}$ ,  $[K_2S_2O_8] = 0.001 \text{ mol/L}$ ,  $[NaHCO_3] = 0.001 \text{ mol/L}$ ,  $[NaHSO_3] = 0.001 \text{ mol/L}$ ,  $[NaCl] = 0.001 \text{ mol/L}$ ,  $[NaBr] = 0.001 \text{ mol/L}$ ,  $[NaI] = 0.001 \text{ mol/L}$ ,  $[NaNO_3] = 0.001 \text{ mol/L}$ ,  $[Na_2SO_4] = 0.001 \text{ mol/L}$ ,  $[Na_2CO_3] = 0.001 \text{ mol/L}$ ,  $[Na_2C_2O_4] = 0.001 \text{ mol/L}$ ,  $[Na_2B_4O_7] = 0.001 \text{ mol/L}$ ,  $[Na_2SiO_3] = 0.001 \text{ mol/L}$ ,  $[Na_2PO_3] = 0.001 \text{ mol/L}$ ,  $[Na_2P_2O_7] = 0.001 \text{ mol/L}$ ,  $[Na_2P_4O_{10}] = 0.001 \text{ mol/L}$ ,  $[Na_2V_2O_7] = 0.001 \text{ mol/L}$ ,  $[Na_2VO_4] = 0.001 \text{ mol/L}$ ,  $[Na_2MoO_4] = 0.001 \text{ mol/L}$ ,  $[Na_2WO_4] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_7] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_8] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_9] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{10}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{11}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{12}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{13}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{14}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{15}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{16}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{17}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{18}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{19}] = 0.001 \text{ mol/L}$ ,  $[Na_2Cr_2O_{20}] = 0.001 \text{ mol/L}$ .